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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/551,298	09/23/2005	Andreas Bergmann	2582.010	3226

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EXAMINER	
FOSTER, CHRISTINE E	

ART UNIT	PAPER NUMBER
1641	

NOTIFICATION DATE	DELIVERY MODE
01/25/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

docketing@mwzb.com

Office Action Summary	Application No.	Applicant(s)	
	10/551,298	BERGMANN ET AL.	
	Examiner	Art Unit	
	Christine Foster	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 October 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,13,14,16 and 18-70* is/are pending in the application.

4a) Of the above claim(s) *13,14,18 and 30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-11,16,19-29 and 31-70* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *9/23/05* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/9/2009 and as corrected in the Reply of 10/7/2009 has been entered.

2. New claims 33-70 have been added. Applicant's clarification is requested in regards to which claims are readable on the elected species of **cardiac disease**. See the Restriction requirement mailed 12/11/2007 (see page 2, "The reply must also identify the claims readable on the elected species, including any claims subsequently added"). Specifically, it is noted that new claims 34 and 38 refer to the disease *sepsis*. **Applicant's clarification is needed as to whether these newly added claims read on the elected species of *cardiac disease*.**

3. Furthermore, the previously examined claims referred only to "cardiac diagnosis" (see claims 15-16). Newly added claim 39 recites a method of diagnosis but also encompasses a method of *prognosis* as well as a method of *therapy-accompanying monitoring of disease*. Similarly, claims 24 and 26-27 have been currently amended so as to refer to *prognosis* and to *therapy-accompanying monitoring of disease*.

In view of this newly added subject matter, the following supplemental election of species requirement is deemed necessary prior to further examination.

Election/Restrictions

4. This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are as follows:

a. Diagnosis of disease

b. Prognosis of disease

c. Therapy-accompanying monitoring of disease

See claims 24, 26-27, and 39.

Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

5. The claims are deemed to correspond to the species listed above in the following manner: Claim 16 reads on species (a). The following claim(s) are generic: claims 1-11, 19-29, and 31-70 appear to be generic.

6. The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons:

According to PCT Rule 13.2, unity of invention exists only when the shared same or corresponding technical feature is a contribution over the prior art. In the instant case, the various different clinical purposes of the methods (diagnosis, prognosis, therapy-accompanied monitoring) share in common the feature of detecting SEQ ID NO:3 in a biological fluid sample for clinical purposes.

However, this feature is not found to represent a contribution over the prior art in view of Valkirs et al. (U.S. 2003/0109420 A1), Richards et al. ("Plasma N-Terminal Pro–Brain Natriuretic Peptide and Adrenomedullin" Circulation 1998;97;1921-1929), and Qi et al. ("Effects of different peptide fragments derived from proadrenomedullin on gene expression of adrenomedullin gene" Peptides 23 (2002) 1141–1147).

Valkirs et al. teach cardiac markers and uses thereof in diagnostic methods (see in particular the abstract). The reference discusses how markers themselves or alternatively, immunologically detectable fragments thereof can be used as targets for screening patient test samples [0018]. For example, addition to detecting a marker itself, one or more fragments of a particular marker or its biosynthetic parent may be detected as a surrogate for the marker itself.

Valkirs et al. illustrate this concept in the case of the marker BNP, which is synthesized from a longer BNP precursor that is proteolyzed to form mature BNP and a remaining fragment (ibid and [0056]). Valkirs et al. teach that addition to mature BNP itself, the longer precursor as well as the remaining fragment can also be used as markers (ibid).

Valkirs et al. do not specifically teach detecting mid-proAM (SEQ ID NO:3).

Qi et al. teach different peptide fragments derived from preproadrenomedullin (title and abstract). In addition to the 52-amino acid peptide adrenomedullin, three other important peptides are produced from this common precursor (page 1141, right column). One of these important peptides is preproADM$_{45\text{-}92}$ (i.e., mid-proAM as recited instantly).

Richards et al. also relates to cardiac markers, focusing on the BNP fragment N-BNP and the 52-amino acid peptide adrenomedullin (see entire selection, in particular abstract and first page). Richards et al. correlate both of these peptides with clinical outcome for patients after myocardial infarction.

In light of the teachings discussed above, it would have been obvious to one of ordinary skill in the art to detect mid-proAM in a biological fluid sample by combining the reference teachings in the following manner. In particular, the teachings of Valkirs et al. suggest that a marker itself, or alternatively fragments of its biosynthetic parent, may be detected in body fluid samples as a diagnostic marker.

Although Valkirs et al. does not specifically contemplate detection of *mid-proAM*, as taught by Qi et al. mid-proAM was known in the prior art to be a fragment of the biosynthetic parent of adrenomedullin (i.e., both adrenomedullin and mid-proAM are important peptide fragments of the same biosynthetic parent molecule, preproadrenomedullin). Adrenomedullin was itself recognized in the prior art to be a marker of clinical interest to human disease, as taught by Richards et al. Consequently, based on the prior art teachings one would be motivated to detect either adrenomedullin itself or fragments of the same biosynthetic parent as markers. As mid-proAM was one of four identified fragments of the adrenomedullin precursor molecule, it

would have been obvious to one of ordinary skill in the art to pursue mid-proAM for detection by selecting from a finite number of identified, predictable solutions.

For these reasons, the feature of detecting mid-proAM in biological fluid is not considered to represent a contribution over the prior art. Consequently, the species of different clinical purposes are not linked by a common special technical feature.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement may be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To preserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

7. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine Foster whose telephone number is (571) 272-8786. The examiner can normally be reached on M-F 7:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on (571) 272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Christine Foster/
Examiner, Art Unit 1641